

REMARKS

Applicants wish to thank the Office for withdrawing the previously lodged claim objections and the rejections maintained under §§112, first paragraph, 102(b), and 103.

**I. Status Of Claims**

Claims 1-23 are pending. Claims 1, and 13 have been amended. The amendments to claims 1 and 13 find support in the specification as filed (*see e.g.*, Example 1, page 15, line 20-page 18, line 15, regarding the capability of subsequent viral infections).

**II. Claim Rejections Under §103**

The Office rejected claims 1-4, 10, 11, 13-15, 21 and 22 under §103 in view of Terwilliger and Liu. Similarly, the Office rejected claims 1-3, 5-9, 11-13, 15-19, and 23 under §103 in view of Terwilliger (for the reasons set forth for claims 1-4, 10, 11, 13-15, 21 and 22) in further view of Liu, Gibbs, Shi, Collman, and/or Li.

Applicants respectfully traverse the Office's position(s). Applicants amended claims 1 and 13 from which all pending claims ultimately depend. Applicants submit that the instant amendments overcome the positions maintained by the Office.

Applicants amendments to claims 1 and 13 adds the recitation "and wherein said vector is capable of initiating multiple rounds of viral infection." As reflected on pages 15 (line 20) through 18 (line 15) of Applicants' specification, Applicants' vectors demonstrated the ability to pass from infected cell cultures to initiate multiple rounds of replication in fresh cell cultures which established the superior replication competence of Applicants' vectors. The replication activity of Applicants' vectors was compared to another vector, and the data from this experiment was reported in the specification (*see page 17, line 10-page 18, line 15*). For ease of consideration, the excerpt from the specification is provided below.

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The replication ability of the NL4Rluc and JRFNRLuc viruses were then compared to that of the JRFNFLuc virus. JRFNFLuc differs from JRFNRLuc in that it encodes the firefly luciferase gene instead of the renilla luciferase gene. JRFNFLuc was constructed in a fashion similar to that previously reported (Chen et al., 1994). Infection of T-cell lines by JRFNFLuc was carried out exactly as that was done for NL4Rluc and JRFNRLuc viruses. As shown in Fig. 9, infection of cells with JRFNFLuc resulted in the production of firefly luciferase activity that was over 200-fold what was observed in uninfected cells 3 days after infection. However, the level of activity did not increase beyond this point in time and p24 activity never increased above background levels during the course of 6 days. The results indicate that mature virus core particles were not being made. Upon passing the day 6 post infection JRFNFLuc supernatant onto uninfected MT-2 #18 cells, no firefly luciferase activity or p24 production could be detected up to seven days post inoculation (data not shown). The results suggest that the supernatants did not contain virus capable of initiating new rounds of replication. Finally, the non-nucleoside reverse transcriptase inhibitor Efavirenz inhibited JRFNFLuc with an effective concentration 50 (EC 50) value of 0.18 nM but the HIV-1 protease inhibitor Amprenavir was unable to inhibit this virus at 10uM; a concentration that is over 1000 fold that of the replication competent JRFNRLuc (Table 1). The finding that this virus was not capable of inhibition by a late stage HIV-1 replication cycle inhibitor is further evidence of it not being able to replicate. Taken together, these data strongly suggests that the JRFNFLuc virus is only capable of a single round of infection and is not replication competent, whereas NL4Rluc and JRFNRLuc are capable of multiple rounds of infection and are bona fide replication competent proviruses.

As described in the specification, the data reflect that Applicants' vectors are capable of more than a single round of infection and demonstrate superior replication properties. There is no teaching or suggestion in the references relied upon by the Office, alone or in combination, of vectors that are capable of more than a single round of infection and are useful for high throughput screening of compounds that modulate various stages of viral infection and/or replication. As a result, the references cited by the Office, alone or in combination, would not have taught each of the elements of Applicants' claims and thus do not rise to the level of establishing a *prima facie* case of obviousness. Accordingly, Applicants submit that the withdrawal of the rejections under §103 is appropriate and is, therefore, respectfully requested.

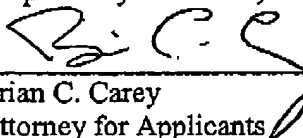
Based on the foregoing, Applicants respectfully submit that the claims are in condition for allowance. Please direct any questions concerning this Response or any aspect of this case to the

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undersigned attorney. The Commissioner is hereby authorized to charge any additional fees which may be required, or credit any overpayment, to Account No. 19-3880 in the name of Bristol-Myers Squibb Company.

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